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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
| 09/016,737 | 01/30/98 | MURPHY | G 8511-007 |

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EXAMINER

DAVIS, M

ART UNIT PAPER NUMBER

1642

DATE MAILED: 06/19/01

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.
09/016,737

Applicant(s)
Murphy et al

Examiner
Minh-Tam Davis

Art Unit
1642



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED on 12/27/00 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY (check only a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.
3. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search. (See NOTE below);
- (b) ☐ they raise the issue of new matter. (See NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: See attached

4. ☐ Applicant's reply has overcome the following rejection(s):

5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).

6. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached

7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):

Claim(s) allowed: NONE

Claim(s) objected to: NONE

Claim(s) rejected: 23, 24, 26, and 28-37

9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.

10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.

11. ☒ Other: A new reference necessary to answer Applicant's arguments is attached.

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Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant amends claims 23 and 28 and adds new claims 31-37, which are related to claims 23-24, 26 and 28-30 and are not new matters.

However the amendment is not entered, because the amended claims 23, 28 and new claims 31-37 present new issues. That is 1) the language "activate T cells to a prostate antigen" of claim 23 is indefinite, and 2) The issues of "20 fold more dendritic cells", "T cells are CD4+ or CD8+" and "dendritic cells are HLA-matched for a recipient" require new rejections.

The following are the remaining rejections.

REJECTION UNDER 35 USC 102

If the amendment were to be entered, rejection under 35 USC 102(e) of claims 23, 24 pertaining to anticipation by Cohen et al would remain for reasons already of record in paper No.11.

Applicant argues that the dendritic cells by Cohen et al, after treatment with calcium ionophore are activated, i.e. mature, and thus cannot process and present antigen. Applicant again

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recites the reference by Pinkl which teaches that cells having a membrane antigen phenotype of a dendritic cell without other data can lack the ability to present antigen. Applicant further asserts that on lines 31-36 column 5 of Cohen, the method by Cohen et al converts monocytes to activated dendritic cells. Applicant recites a new reference by Koch et al, which teaches that population of mature dendritic cells are heterogenous, and include small number of immature dendritic cells. Koch et al further teach that mature dendritic cells down regulate their processing capacity, whereas the subset of immature dendritic cells could handle native protein Ag. Applicant asserts that a small population of immature dendritic cells would not be present in the composition of Cohen et al, because Cohen et al describe their dendritic cells as being a homogenous population of activated or mature dendritic cells. Applicant further recites the reference by Czerniecki et al, 1997, co-authored by Cohen and several inventors in the cited reference by Cohen et al, which teaches the activation of dendritic cells by calcium ionophore, and still studies the ability of MOMC treated with calcium ionophore to sensitize autologous T cells *in vitro*. Further, Applicant argues that as newly amended, the instant invention is patentably distinct from Cohen et al.

Applicant's arguments set forth in paper No.14 have been considered but are not deemed to be persuasive for the following reasons:

The recitation of Pinkl, Koch et al, and Czerniecki et al is acknowledged. It seems that Applicant misinterpretes the word "activated" dendritic cells used by Cohen et al as "mature" dendritic cells. Cohen et al teach that certain specific combination of cytokines have been used

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successfully to amplify or partially substitute for the activation/conversion achieved with calcium ionophore. These cytokines include rhGM-CSF, rhIL-2, reIL-4 and rhIL-12. Each cytokine when given alone is inadequate for optimal upregulation (column 10, lines 54-60). Sallusto, F et al, 1994, J Exp Med, 179: 1109-1118, teach that the exposure to Granulocyte/Macrophage colony-stimulating factor plus interleukin 4 converts blood mononuclear cells to dendritic cells, and that cultured, isolated dendritic cells when maintained by Granulocyte/Macrophage colony-stimulating factor plus interleukin 4 could efficiently present soluble antigen. Thus it seems that Cohen et al use the language "activation" the same as "conversion", and that exposure to calcium ionophore gives the same result as to exposure to cytokines. As evidenced by Salluto et al, one of ordinary skill in the art would have expected that the dendritic cells taught by Cohen et al would process and present antigen, similar to dendritic cells previously exposed to cytokines. Further, as recited in previous Office action, in example 2 of Cohen et al, the dendritic cells have been successfully used for reducing prostate tumor size (column 12, lines 27-32). Thus one of ordinary skill in the art would have expected that the dendritic cells taught by Cohen et al are fully functional, i.e. processing and presenting antigen, and activating specific T cells which are expected to be responsible for reducing tumor growth. Further, Applicant is arguing limitations not recited in the claims as presently constituted, since the submitted amendment has not been and will not be entered.

REJECTION UNDER 35 USC 103

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1. If the amendment were to be entered, rejection under 35 USC 103 of claim 26 pertaining to obviousness over Cohen et al in view of Lutz et al would remain for reasons already of record in paper No.11.

Applicant argues that as newly amended, the instant invention is patentably distinct from the dendritic cells of Cohen et al for the reasons set forth above. Further, Applicant argues that the dendritic cells taught by Cohen et al do not process and present antigen. Thus the reference by Lutz et al adds nothing to render the claim obvious.

Applicant's arguments set forth in paper No.14 have been considered but are not deemed to be persuasive for the following reasons:

The claimed dendritic cells are not patentably distinct from the dendritic cells of Cohen et al for the reasons set forth above. Further, one of ordinary skill in the art would have expected that the dendritic cells taught by Cohen et al process and present antigen.

2. If the amendment were to be entered, rejection under 35 USC 103 of claims 28, 29 pertaining to obviousness over Cohen et al in view of Taylor et al would remain for reasons already of record in paper No.11.

Applicant argues that as newly amended, the instant invention is patentably distinct from the dendritic cells of Cohen et al for the reasons set forth above. Further, Applicant argues that the dendritic cells taught by Cohen et al do not process and present antigen. Thus one cannot combine the two references.

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Applicant's arguments set forth in paper No.14 have been considered but are not deemed to be persuasive for the following reasons:

The claimed dendritic cells are not patentably distinct from the dendritic cells of Cohen et al for the reasons set forth above. Further, one of ordinary skill in the art would have expected that the dendritic cells taught by Cohen et al process and present antigen.

3. If the amendment were to be entered, rejection under 35 USC 103 of claim 30 pertaining to obviousness over Cohen et al in view of Taylor et al, further in view of Lutz et al would remain for reasons already of record in paper No.11.

Applicant argues that as newly amended, the instant invention is patentably distinct from the dendritic cells of Cohen et al for the reasons set forth above. Further, Applicant argues that the dendritic cells taught by Cohen et al do not process and present antigen. Thus none of the added references suggest or disclose the claimed invention.

Applicant's arguments set forth in paper No.14 have been considered but are not deemed to be persuasive for the following reasons:

The claimed dendritic cells are not patentably distinct from the dendritic cells of Cohen et al for the reasons set forth above. Further, one of ordinary skill in the art would have expected that the dendritic cells taught by Cohen et al process and present antigen.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The

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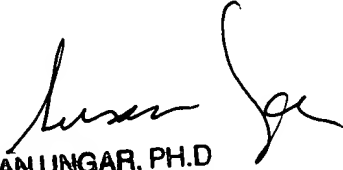
examiner can normally be reached on Monday-Friday from 9:30am to 3:30pm, except on Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

June 10, 2001



SUSAN UNGAR, PH.D
PRIMARY EXAMINER